diagnose as the signs and symptoms are distinctive. On the other hand, less symptomatic or asymptomatic cases of hereditary hemochromatosis are likely to be underappreciated. Some of the early symptoms of hemochromatosis—weakness, lethargy, loss of libido, arthralgia—may be indistinguishable from those of more common disorders, and clinicians may need to consider hemochromatosis more frequently in the presence of these.[2] The patient's age or sex should not be a reason to exclude hereditary hemochromatosis from the differential diagnosis.

Screening for hemochromatosis is accomplished relatively easily. Some authors have advocated that the iron status of every patient be screened to evaluate for both iron overload and iron deficiency.[6] Although physicians may not consider measuring iron levels and total iron-binding capacity on every patient, they should keep in mind that hemochromatosis may be more prevalent than they think. It is important to prevent or reverse the complications of hemochromatosis with appropriate management during the early clinical stages.[12] It is especially important to note that women of childbearing age are not always protected from the clinical consequences of hereditary hemochromatosis, as exemplified by this case report.

We have described a common disorder with a rare presentation. Apparently no group is completely protected from this disease, including young women. Because the consequences of hereditary hemochromatosis are preventable or reversible to some degree with prompt treatment, early recognition of the disease is vital. Our case shows that a patient's being young or female should not be a reason to exclude hereditary hemochromatosis from the differential diagnosis when findings are suggestive of this disorder.

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Multiple Stress Fractures
An Unusual Presentation of Cushing's Disease

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STRESS FRACTURES occurring as a result of overzealous sports activities have become commonplace, but multiple stress fractures other than in a symmetric distribution are unusual. In the case reported here, the finding of multiple areas of abnormal uptake on a bone scan might have been mistaken for metastatic disease. Additional questioning of the patient and the often-requested "clinical correlation" led to the correct diagnosis of Cushing's disease. This case emphasizes the importance of the clinical history and the correlation of plain radiographs in interpreting skeletal scintigraphic findings.

Report of a Case

The patient, a 30-year-old woman, was seen initially with bilateral hip pain of one month's duration. The pain radiated to the groin and was aggravated on rising from a seated position. She had carried a diagnosis of schizoaffective disorder for the previous nine years. Her current medications were haloperidol, 10 mg at bedtime; trazodone hydrochloride, 300 mg at bedtime; and lorazepam, 0.5 mg twice a day.

An anteroposterior film of the pelvis showed an unusual crescentic lucency over the left pubis, resembling a "vacuum phenomenon" (Figure 1), and bilateral degenerative changes at the hips. Also noted was diffuse osteopenia. The rest of the pelvis was judged unremarkable, although visualization of the sacroiliac joints was suboptimal because of the patient's body habitus. A bone scan was recommended because the unusual appearance of the pubic lesion suggested the possibility of pathologic fracture.

The bone scan (Figure 2) showed multiple foci of abnormal tracer uptake consistent with fractures involving C-7, several ribs, the sacrum and sacroiliac joints, both iliac fossae, and the left superior and inferior pubic rami. Also noted were areas of increased activity along the medial proximal tibial diaphysis and in the metatarsal bones (Figure 3). On further questioning in the nuclear medicine department, the patient reported that for the past month

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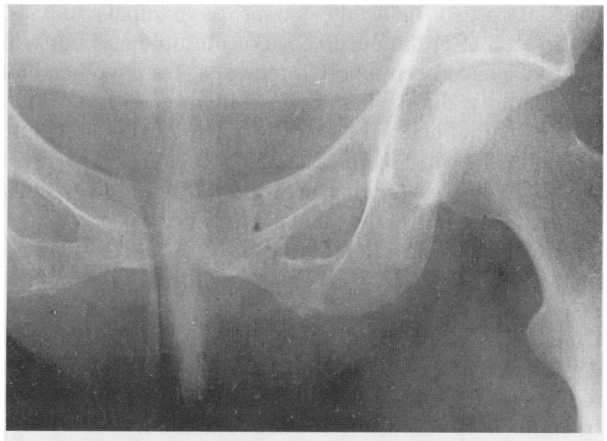

Figure 1.—The detail of an anteroposterior radiograph of the pelvis shows a left superior pubic ramus fracture with a vacuum phenomenon.

she had engaged in daily three-hour, high-intensity aerobic exercise and walking in an attempt to lose weight. On review of her medical record, the following were noted: a 6.8-kg (15-lb) weight gain over the past two years, easy bruising for the past five years, worsening acne, and a rounded, somewhat reddish face. Correlation with the available plain radiographs suggested multiple stress fractures and, in this case, insufficiency fractures due to osteoporosis.

The finding of multiple insufficiency fractures on the bone scan, additional history, and the patient's cushingoid appearance prompted further workup for presumed Cushing's syndrome. The AM serum cortisol level was mildly elevated, and the 24-hour urine cortisol level was markedly elevated at 2,200 nmol per day (normal, 30 to 300 nmol per day). A serum corticotropin (formerly

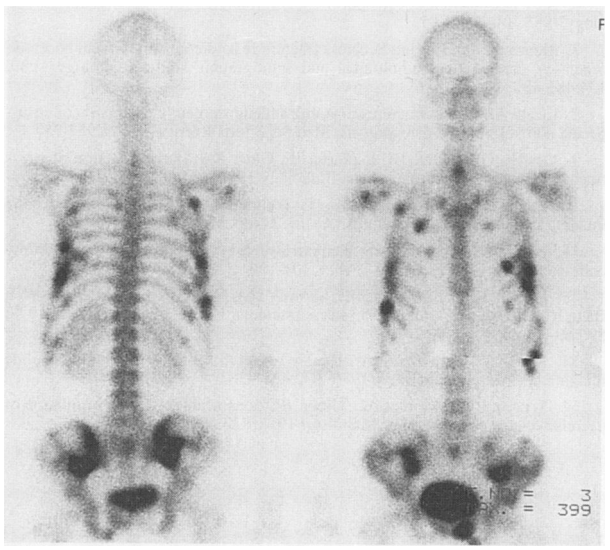

Figure 2.—Posterior and anterior views of the bone scan reveal multiple foci of increased uptake in the anterior C-7 vertebra, ribs, sacrum, sacroiliac joints, iliac fossae, and the superior and inferior left pubic rami.

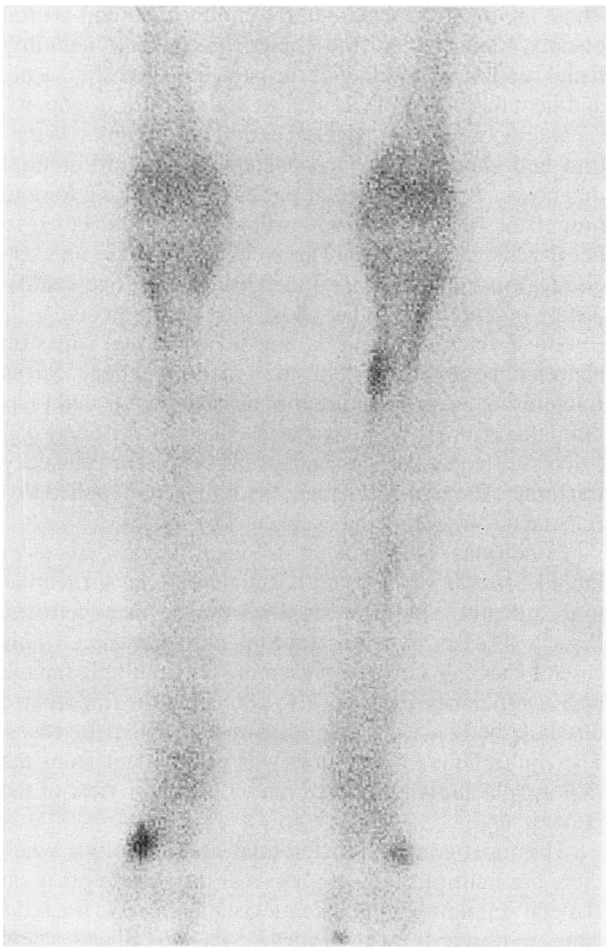

Figure 3.—An anterior view of a lower extremity bone scan shows stress phenomena, including two areas in the proximal and midleft tibial diaphysis, and in the metatarsal bones bilaterally.

ACTH) level was measured at 13 pmol per liter (normal, 4 to 22 pmol per liter), and the results of subsequent dexamethasone suppression testing, low- and high-dose, as well as corticotropin-releasing hormone and metyrapone testing, were all consistent with a diagnosis of pituitary Cushing's disease. This was confirmed by magnetic resonance imaging of the sella, which showed a 5-mm pituitary adenoma. The patient underwent transsphenoidal resection. The histologic diagnosis was amphophilic corticotropin-producing pituitary adenoma.

Following the resection, her cortisol and corticotropin values fell to normal levels. Now, two years after her operation, she is doing well, has lost 9 kg (20 lb), and has no laboratory evidence of hormonal imbalance. Her psychiatric symptoms persist, and she has continued on her psychiatric medications.

Discussion

Cushing's syndrome is the clinical and metabolic disorder resulting from glucocorticoid excess. Cushing's disease refers to the condition where excess corticotropin is secreted due to hypothalamic-pituitary dysfunction.

There are many clinical manifestations, including central obesity, moon facies, and cutaneous changes including facial ruddiness, thinning of the skin, easy bruising, acne, and hirsutism. Notable as well in this case are osteoporosis and mood alterations. Depression is a common symptom and should also be considered in the differential diagnosis.[1] In this particular patient, it is striking to note how many of her symptoms were possibly attributed to her psychiatric diagnosis. Her weight gain led to an exercise regimen that in turn led to multiple stress and insufficiency fractures due to her underlying osteoporosis.

Stress fractures occur as a result of normal stress on abnormal bone or abnormal stress on normal bone. Stress fractures occurring in normal bone may be referred to as fatigue fractures, whereas those occurring in abnormal (such as osteoporotic) bone are usually called insufficiency fractures.[2] The term pathologic fracture is best applied to a fracture occurring in bone weakened by tumor.[3]

Conditions predisposing to insufficiency fractures include osteoporosis, osteomalacia and rickets, rheumatoid arthritis, osteogenesis imperfecta, osteopetrosis, Paget's disease, hyperparathyroidism, and others.[3] This case of Cushing's disease presenting with multiple fatigue and insufficiency fractures also points out the importance of whole-body skeletal scintigraphy in problematic cases. The multiplicity of fractures was not evident from the radiographs initially ordered (anteroposterior view of the pelvis).

The most common differential considerations when there are multiple sites of abnormal increased uptake on skeletal scintigraphy include metastatic disease, fractures from multiple trauma, arthritis, Paget's disease, and postsurgical changes. Less common considerations would include aseptic necrosis, polyostotic fibrous dysplasia, lymphoma, multiple myeloma, hematogenous osteomyelitis, metabolic bone disease, multifocal primary bone tumors, and stress fractures.[4] The pattern of abnormal uptake may suggest the clinical disorder such as medial knee joint involvement in osteoarthritis or the linear distribution of multiple contiguous rib fractures.

Most stress fractures occur in the lower limbs, particularly in the tibias, and less commonly in the femurs and the feet (metatarsals, sesamoids, navicular, calcaneus). Rare stress fracture sites, as seen in this case, include the pubic and sacroiliac joint regions and ribs.[5] Osteoporotic insufficiency fractures may occur in the sacrum and are often radiographically occult.[6] Multiple stress fractures are unusual, except in the case of insufficiency fractures resulting from systemic disease and in bilateral symmetrical stress fractures in the lower limbs.[7] Two additional cases of cortisol-induced osteoporosis in female athletes, discovered after the occurrence of multiple and unusual fractures, have been reported recently.[8] Both women had substantially diminished bone mineral density, which showed partial reversal following therapy. Although bone densitometry was recommended in our case, it was never requested by the clinicians. It is doubtful that the results would have changed the patient's treatment.

The bone scan remains the most sensitive imaging modality to diagnose stress-related injuries to bone.[9-11] As in other osseous pathologic processes—metastases, osteomyelitis, infarction—scintigraphy has the potential for demonstrating lesions and multiplicity earlier than roentgenography.[12,13] In addition, certain sites of stress fractures have characteristic scintigraphic findings ranging from an ill-defined cortical area of increased radiotracer uptake to an extensive transcortical area of intense increased activity.[5,13,14]

Our patient's report of exuberant exercise activity, combined with the pattern of abnormalities and the confirmatory plain film findings, led to the correct conclusion of multiple stress fractures—both fatigue and insufficiency fractures related to underlying osteoporosis. It remained for her clinicians to determine the predisposing disease state and to make the final diagnosis of Cushing's disease.

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